REMARKS

The Applicants appreciate the Examiner's thorough examination of the subject application. Applicants request reconsideration of the subject application based on the amendments to the claims and the following remarks.

Claims 1 – 29 are currently pending in the application. Claims 1, 16 and 17 have been amended. Claims 15 has been withdrawn.

Support for the amendments to the claims can be found throughout the application as filed. No new matter has been added by the amendments to the specification or the claims.

More particularly, in the currently outstanding Official Action:

1. Claims 4, 6, 8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The Examiner states that "Claim 4, 6, 8 recites the limitation "the dosage" in line 1. There is insufficient antecedent basis for this limitation in the claim.".

Applicants have amended Claim 1 to provide antecedent basis for the phrase, "the dosage" in Claims 4, 6 and 8. As such, Applicants believe the rejections have been obviated and respectfully request reconsideration.

2. Claims 1,2,7,9,10,15,19,20,23,24 are rejected under 35 U.S.C. 102(b) as being anticipated by Pocchiari et al (Hormone Research, 19991, vol. 35 no. 3-4, pp. 161-6). The Examiner states that "Pocchiari teaches a method of treating prion disease (scrapie) in human comprising administering a prion protein denaturing effective agent (6 M urea) to the human. It is inherent that the administration of the 6 M urea would induce hyperthermia. See abstract.".

Applicants respectfully disagree and submit that the law of anticipation is well settled to the effect that:

> "A claim is **anticipated** only if **each and every** element as set forth in the claim is found either expressly or inherently described in a single prior art reference" *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987), MPEP 2131.
> (Empahsis added)

Applicants respectfully submit that this standard is not met when the Pocchiari reference is relied upon by the Examiner and compared with the invention claimed herein. The Pocchiari reference describes the effect of 6M Urea on the infectivity of human pituitary tissue that had been deliberately contaminated with scrapie virus. Nowhere in the reference does Pocchiari describe the use of Urea for the administration to a mammal in the treatment of a prion disease. As such, Applicants believe the rejection is inappropriate and respectfully request reconsideration.

3. Claims 1-3,9,10,13-15,19-21,23,24,27-29 are rejected under 35 U.S.C. 102(b) as being anticipated by Manuelidis et al (Proceeding of the National Academy of Sciences of USA, 1995, vol. 92 no. 11 pp. 5124-8). The Examiner states that "Manuelidis teaches a method of treating prion diseases: scrapie in sheep; and Creutzfeldt-Jakob (CJD) disease in human, comprising administering a prion protein denaturing effective agent (guanidine hydrochloride) to the mammals. It is inherent that the administration of the guanidine hydrochloride would induce hyperthermia. See abstract.".

Applicants respectfully submit that the standard of anticipation is not met when the Manuelidis reference is relied upon by the Examiner and compared with the invention claimed herein. The Manuelidis reference relates to the *in vitro* treatment of prion proteins with guanidine hydrochloride to evaluate the effect of guanidine hydrochloride on the infectivity of prion protein. Nowhere in the reference does Manuelidis describe the use of guanidine hydrochloride for the administration to a mammal in the treatment of a prion disease. As such, Applicants believe the rejection is inappropriate and respectfully request reconsideration.

4. Claims 1,2,7-15,19,20,22-29 are rejected under 35 U.S.C. 102(b) as being anticipated by Madec et at (Archives of Virology, 1997, vol. 142 no. 8, pp. 1603-1612). The Examiner states, "Madec teaches a method of treating prion diseases: scrapie in sheep; bovine spongiform encephalopathy in cows; and Creutzfeldt-Jakob disease in human, comprising administering a prion protein denaturing effective agent (1-7 M urea and 0.25-3 M guanidine thiocynate) to the mammals. It is inherent that the administration of the urea and guanidine thiocyanate would induce hyperthermia. See abstract."

Applicants respectfully submit that the standard of anticipation is not met when the Madec reference is relied upon by the Examiner and compared with the invention claimed herein. The Madec reference relates to the *in vitro* treatment of prion proteins with urea or guanidine thiocyanate to evaluate the their effect on the protease resistance of prion proteins. Nowhere in the reference does Madec describe the use of urea or guanidine thiocyanate for the administration to a mammal in the treatment of a prion disease. As such, Applicants believe the rejection is inappropriate and respectfully request reconsideration.

5. Claims 1,2,9,10,15,19,20,23,24 are rejected under 35 U.S.C. 102(b) as being anticipated by Goldin et al (US 5403861; 4/4/95). The Examiner states that "Goldin teaches a method of treating prion disease (insomnia) in human comprising administering a prion protein denaturing effective agent (guanidine salt) to the human. It is inherent that the administration of the guanidine would induce hyperthermia. See abstract, column 8 line 64 – column 9 line 20.".

Applicants respectfully submit that the standard of anticipation is not met when the Goldin reference is relied upon by the Examiner and compared with the invention claimed herein. The Goldin reference teaches guanidine based structures and their use for the treatment or prevention of pathophysiologic conditions characterized by the release of excessive or inappropriate levels of neurotransmitters. Nowhere in the reference does Goldin describe the use of a prion protein denaturing effective agent or guanidine based structures for the administration to a mammal in the treatment of a prion disease. The Examiner specifically refers to "insomnia" as a prion disease. Although insomnia may or may not be a symptom of a prion disease, insomia is clearly not considered a member of the

diseases that are caused by the transmission of a prion protein. As such, Applicants believe the rejection is inappropriate and respectfully request reconsideration.

6. Claims 1,2,9,10,13-15,19,20,23,24,27-29 are rejected under 35 U.S.C. 102(e) as being anticipated by Garssen et al (WO 0048003; 8/17/00). The Examiner states that "Garssen teaches a method of treating prion diseases: scrapie; spongiform encephalopathy; fatal familial insomnia; kuru; Gerstmann-Straussler-Scheinker disease (GSS) and CJD in human and animals, comprising administering a prion protein denaturing effective agent (1-7 M urea and 0.25-3 M guanidine thiocynate) to the mammals. It is inherent that the administration of the urea and guanidine thiocyanate would induce hyperthermia.".

Applicants respectfully submit that the standard of anticipation is not met when the Garssen reference is relied upon by the Examiner and compared with the invention claimed herein. The Garssen reference teaches the use of guanidine thiocyanate for treating a sample in a diagnostic method for reducing the risk of scoring a false positive test result for the presence of prion protein. Nowhere in the reference does Garssen describe the use of guanidine thiocyanate for the administration to a mammal in the treatment of a prion disease. As such, Applicants believe the rejection is inappropriate and respectfully request reconsideration.

7. Claims 1-3,7,9-11,13-15,19-21,23,24,27-29 are rejected under 35 U.S.C. 102(e) as being anticipated by Chang et al (US 2002/0132268; 9/19/02). The Examiner states that "Chang teaches a method of treating prion diseases: scrapie in sheep; CJD in human; GSS in human; familial insomnia in human; and kuru in human, comprising administering a prion protein denaturing effective agent (urea and guanidine chloride) to the mammals. It is inherent that the administration of the urea and guanidine chloride would induce hyperthermia. See abstract, page 8 paragraphe 107, claims 48-50."

Applicants respectfully submit that the standard of anticipation is not met when the Chang reference is relied upon by the Examiner and compared with the invention claimed herein. The Chang reference teaches methods of making prion isomers, compositions

comprising prion isomers, antibody compositions to a prion isomer, methods of screening a patient for a neurodegenerative disease and methods for treating a patient afflicted with a neurodegenerative disease. The methods of treatment for neurodegenerative diseases disclosed in Chang, however, relate to the use of antibodies directed to prion isomers and not to the use of prion protein denaturing effects. Nowhere in the reference does Chang describe the use of a prion protein denaturing effective agent for the administration to a mammal in the treatment of a prion disease. As such, Applicants believe the rejection is inappropriate and respectfully request reconsideration.

8. Claim 8 is rejected under 35 U.S.C. 103(a) as being unpatentable over Pocchairi as applied to claims 1,2,7,9,10,15,19,20,23,24. See Pocchairi 35 USC 102(b) rejection above. The Examiner states that "Pocchairi teaches all that is recited in claim 8 except for the invention comprising the instant amount of urea. It would have been obvious to one having ordinary skill in the art to determine the optimum amount of urea. One would have been motivated to do this in order to make an invention that would have been most effective in treating prion disease.".

Applicants respectfully disagree for the same reasons stated above in overcoming the anticipation rejection relating to the Pocchairi reference.

9. Claim 4 is rejected under 35 U.S.C. 103(a) as being unpatentable over Manuelidis as applied to claims 1-3, 9,10,13-15,19-21,23,24,27-29. See Manuelidis 35 USC 102(b) rejection above. The Examiner states that "Manuelidis teaches all that is recited in claim 4 except for the invention comprising the instant amount of guanidine hydrochloride. It would have been obvious to one having ordinary skill in the art to determine the optimum amount of guanidine hydrochloride. One would have been motivated to do this in order to make an invention that would have been most effective in treating prion disease.".

Applicants respectfully disagree for the same reasons stated above in overcoming the anticipation rejection relating to the Manuelidis reference.

10. Claim 4 is rejected under 35 U.S.C. 103(a) as being unpatentable over Madec as applied to claims 1,2, 7-15,19,22-29. See Madec 35 USC 102(b) rejection above. The Examiner states that "Madec teaches all that is recited in claim 4 except for the invention comprising the instant amount of guanidine thiocyanate. It would have been obvious to one having ordinary skill in the art to determine the optimum amount of guanidine thiocyanate. One would have been motivated to do this in order to make an invention that would have been most effective in treating prion disease.".

Applicants respectfully disagree for the same reasons stated above in overcoming the anticipation rejection relating to the Madec reference.

11. Claims 4,8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chang as applied to claims 1-3, 7,9-11,13-15,19-21,23,24,27-29. See Chang 35 USC 102(e) rejection above. The Examiner states that "Chang teaches all that is recited in claims 4,8 except for the invention comprising the instant amounts of guanidine chloride and urea. It would have been obvious to one having ordinary skill in the art to determine the optimum amounts of guanidine chloride and urea. One would have been motivated to do this in order to make an invention that would have been most effective in treating prion disease.".

Applicants respectfully disagree for the same reasons stated above in overcoming the anticipation rejection relating to the Chang reference.

These references taken alone or in combination with the other cited references simply do not teach, imply or provide any motivation for developing the treatment of a prion disease with prion protein denaturing effective agents, as Applicants have done.

In summary, therefore, it is believed that the foregoing discussion of the Pocchairi, Manuelidis, Madec, Goldin, Garssen and Chang references in comparison with the present invention clearly and persuasively points out the distinctions between them. It also is respectfully submitted that upon reconsideration of the present application and the cited Pocchairi, Manuelidis, Madec, Goldin, Garssen and Chang references in view of the

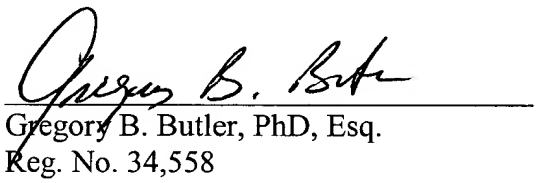
foregoing discussion, the Examiner will agree that the Applicant's invention is clearly and definitely patentably distinct.

For each an all of the foregoing reasons and in view of the foregoing amendment, it is believed that Claims 1-29 as hereinabove amended now are in condition for allowance. Favorable reconsideration and allowance of this application, therefore, is respectfully requested in response to this communication.

Applicants believe that additional fees are not required to complete the filing requirements for the subject application or otherwise in connection with this submission. However, if a fee is required, a fee paid is inadequate or credit is owed for any excess fee paid, you are hereby authorized and requested to charge/credit Deposit Account No. **04-1105.**

Respectfully submitted,

Date: July 13, 2004

By: 

Gregory B. Butler, PhD, Esq.
Reg. No. 34,558

EDWARDS & ANGELL, LLP
P.O. Box 55874
101 Federal Street
Boston, MA 02205
(617) 517-5595
Customer No.: 21874